PON1 L55M SNP as a promising genetic biomarker for predicting response to anti-VEGF treatment

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Purpose

The purpose of this study was to determine whether five inflammation- and oxidative stress-related genetic polymorphisms from three different genes (APOE, PON1, SDF-1) may affect the response to anti-vascular endothelial growth factor (anti-VEGF) treatment in macular oedema secondary to retinal vein occlusion (RVO).

Methods

Participants in this prospective study were 50 treatment-naïve patients with macular oedema secondary to RVO. All patients were treated with intravitreal anti - VEGF agents, either ranibizumab or aflibercept, having a loading phase of 3 monthly injections and PRN thereafter, while all participants had at least 12-month follow-up. The change in best-corrected visual acuity (BCVA) and central subfield thickness (CST) between baseline and month 12 were calculated for each participant.

Genotyping for the genetic polymorphisms was determined by performing Polymerase Chain Reaction – Restriction Fragment Length Polymorphism (PCR – RFLP), using sequence-specific primers for each gene polymorphism.

Results (1)

The LL genotype of the PON1 L55M single nucleotide polymorphism (SNP) provided statistically significantly better anatomical treatment response, as patients with this genotype had higher reduction in CST at month 12 (101.63 $\pm$ 56.80 µm in LL vs. 72.44 ± 39.41 µm in LM vs. 40.25 $\pm$ 19.33 µm in MM, p=0.026) (Figure 1). Patients with the M allele of the PON1 L55M SNP were statistically significantly associated with lower reduction in CST to treatment compared to non-carriers (68.29 $\pm$ 38.77 µm in LM + MM vs. 101.63 $\pm$ 56.80 µm in LL, p = 0.032) (Figure 2).

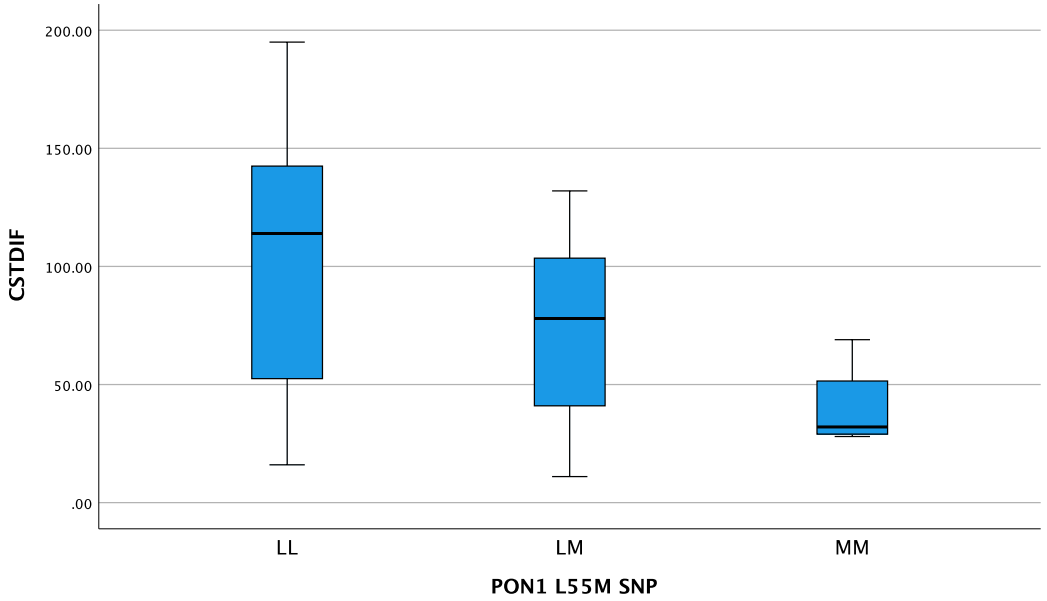

Figure 1. The decrease in central retinal thickness (CSTDIF) between baseline and month 12 in patients with LL, LM and MM genotypes for *PON1* L55M SNP

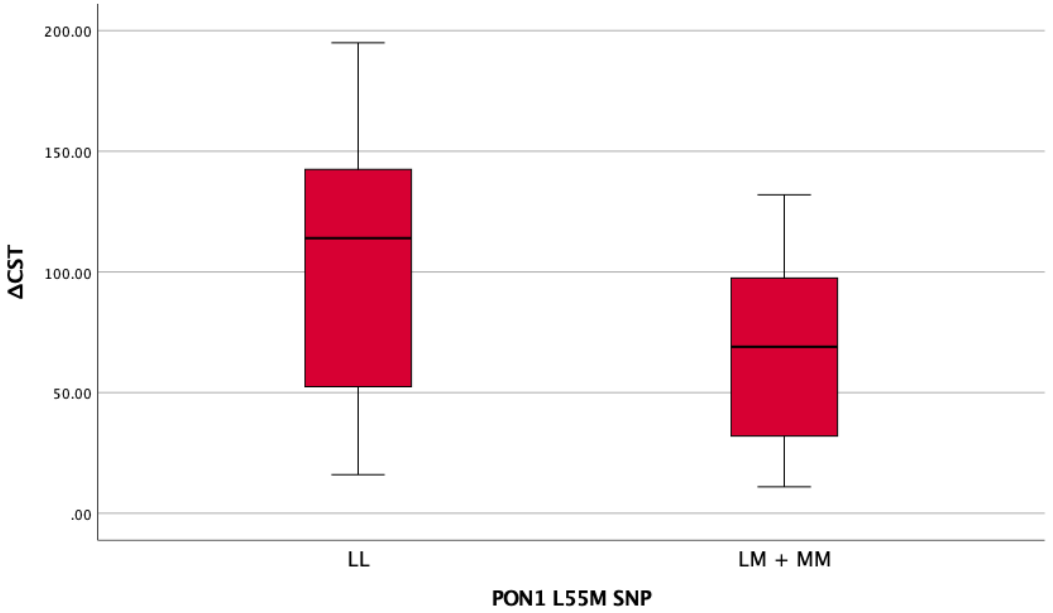

Figure 2. The decrease in central retinal thickness (CSTDIF) between baseline and month 12 in patients with LL genotype and M allele carriers (LM + MM) for *PON1* L55M SNP

Results (2)

No statistically significant difference was found in the functional response as well as the number of injections among the different genotypes or alleles for all the studied genetic polymorphisms. Multivariate linear regression analysis of LL genotype over anatomical treatment response, adjusted for age, sex and baseline CST, was performed. The regression revealed that, even after adjustment, the LL genotype of PON1 L55M had higher reduction in CST after treatment (β = -0.311, p = 0.036). Covariates age, sex and baseline CST did not demonstrate any statistical significance in the regression model.

Conclusions

The presence of the minor M allele of the PON1 L55M SNP was associated with poorer anatomical outcomes after 12-month anti-VEGF treatment for macular oedema secondary to RVO, suggesting that PON1 L55M SNP may serve as a promising genetic biomarker for predicting response to anti-VEGF treatment.